

FIG._ 1A

FIG. 1B - 1

250 Gln Val Arg Ser Ser Leu Glu Asn Thr Thr Lys Leu Gly Asp Ser Phe Tyr Gly Ile Gly Ile Asn
1149 CAA GTC CGC ACC AGT TTA GAA AAC ACC ACT ACA AAA CTT GAT TCT TAC TAT GGA AAA GGG CTG ATC AAC
260
270 Val Gln Ala Ala Gln OC TERM
1224 GIA CAG CGG GCA GCT CAG TAA AACATAAAAACCGGCCCTGGCCGGTTTATTTCTCTCCGGATGTCAATCCCTCC
1316 ATATCGACGGATGGCTCCCTGAAAAATTAAACGAGAACGGGCGCTGACCCCGCTAGTCCTGAAAGTCCTGAAACGTCCTGAAATCGCCG
1416 CTTCGGTTTCCGTCAATGCCGTAAACGGTGGGGGTTCGATACGGGAGACGGCATTCCTAATCGGATC

FIG.- 1B - 3

FIG.-1B - 1

FIG.-1B - 2

FIG.-1B - 3

FIG.- 1B

CONSERVED RESIDUES IN SUBTILISINS FROM
BACILLUS AMYLOLIQUEFACIENS

1	10	20
A Q S V P . G	A P A . H . . G	
21	30	40
. T G S . V K V A V . D . G	H P	
41	50	60
D L . . . G G A S . V P	Q D	
61	70	80
. N . H G T H V A G T . A A L N N S I G		
81	90	100
V L G V A P S A . L Y A V K V L G A . G		
101	110	120
S G . . S . L . . G . E W A . N		
121	130	140
V . N . S L G . P S . S A . .		
141	150	160
. G V . V V A A . G N . G . . .		
161	170	180
. Y P . . Y A V G A .		
181	190	200
D . . N . . A S F S . . G . . L D . . A		
201	210	220
P G V . . Q S T . P G . . Y . . . N G T		
221	230	240
S M A . P H V A G A A A L . . . K . . .		
241	250	260
W . . . Q . R . . L . N T . . . L G . .		
261	270	
. . Y G . G L . N . . A A . .		

FIG._2

COMPARISON OF SUBTILISIN SEQUENCES FROM:

B.amyloliquefaciens

B.subtilis

B.licheniformis

B.lentus

01	A Q S V P Y G V S Q I K A P A L H S Q G Y T G S N V R V A V I D S C I D S S H P	10	A Q S V P Y G V S Q I K A P A L H S Q G Y T G S N V R V A V I D S C I D S S H P	20	A Q T V P Y G I S Q I K A P A L H S Q G Y T G S N V R V A V I D S C I D S S H P	30	A Q T V P Y G I S Q I K A D K V Q A Q G F K G A N V R V A V I D T C I Q A S H P
41	D L K V A G G A S M V P S E T N P P Q D N N S H G T H V A G T V A A L N N S I C	50	D L N V R G G A S P V P S E T N P Y Q D G S S H G T H V A G T I A A L N N S I C	60	D L N V V G G A S P V V A G E A Y N * T D G N G H G G T H V A G T V A A L D N T C	70	D L N I R G G A S P V P G E * P S T Q D G N G H G G T H V A G T I A A L N N S I C
81	V L G V A P S A S S L Y A V K V L G A D G S G Q Y S W I I N G I E W A I A N N M D	90	V L G V S P S A S S L Y A V K V L D S T G S G Q Y S W I I N G I E W A I S N N M D	100	V L G V A P S V S S L Y A V K V L N S S G S S Y S G I V S G I E W A T T N G M D	110	V L G V A P S A E L Y A V K V L G A S G S S V S S I A Q G L E W A G N N G M H
121	V I N M S L G G C P S G S A A L K A A V D K A V A S G V V V A G N E G T S G	130	V I N M S L G G P T G S T A L K T V V D K A V S S G I V V A A A G N E G S S G	140	V I N M S L G G A S G S T A M K Q A V D N A Y A R G V V V A A A G N S G N S G	150	V A N L S L G S P S P S A T L E Q A V N S A T S R G V L V V A A S G N S G A G S

FIG.-3A

161	S S T V G Y P G K Y P S V I A V G A V D S S N Q R A S F S S V G P E L D V M A	170	S S T V G Y P A K Y P S T I A V G A V N S S N Q R A S F S S V G S E L D V M A	179	S S T N T I G Y P A K Y D S V I A V G A V D S N S N R A S F S S V G A E L E V M A	188	S S T N T I S Y P A R Y A N A M A V G A T D Q N N R A S F S S Q Y G A G L D I V A
201	P G V S I Q S T L P G N K Y G A Y N G T S M A S P H V A G A A A L I L S K H P N	210	P G V S I Q S T L P G G T Y G A Y N G T S M A T P H V A G A A A L I L S K H P T	219	P G A G V Y S T Y P T N T Y A T L N G T S M A S P H V A G A A A L I L S K H P N	228	P G V N V Q S T Y P G S T Y A S L N G T S M A T P H V A G A A A L V K Q K N P S
241	W T N T Q V R S S L E N T T K L G D S F Y Y G K G L I N V Q A A A Q	250	W T N A Q V R D R L E S T A T Y L G N S F Y Y G K G L I N V Q A A A Q	259	W T N S A S Q V R N R L S S T A T Y L G S S F Y Y G K G L I N V E A A A Q	268	W T N L S S N V Q I R N H L K N T A T S L G S T N L Y G S G L V N A E A T R
291	W T N L S S N V Q I R N H L K N T A T S L G S T N L Y G S G L V N A E A T R	300	W T N L S S N V Q I R N H L K N T A T S L G S T N L Y G S G L V N A E A T R	309	W T N L S S N V Q I R N H L K N T A T S L G S T N L Y G S G L V N A E A T R	318	W T N L S S N V Q I R N H L K N T A T S L G S T N L Y G S G L V N A E A T R

FIG. 3B

FIG. 3

FIG. 3B

FIG. 4

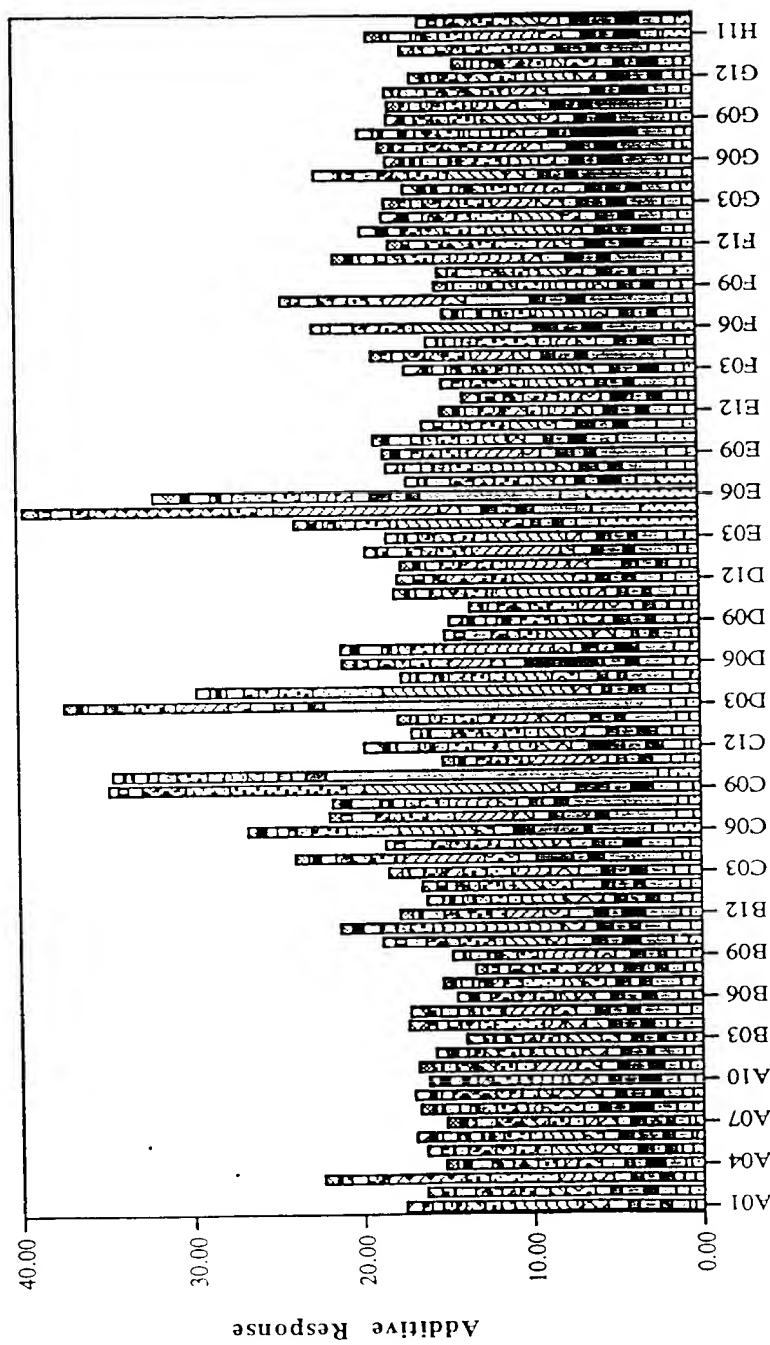
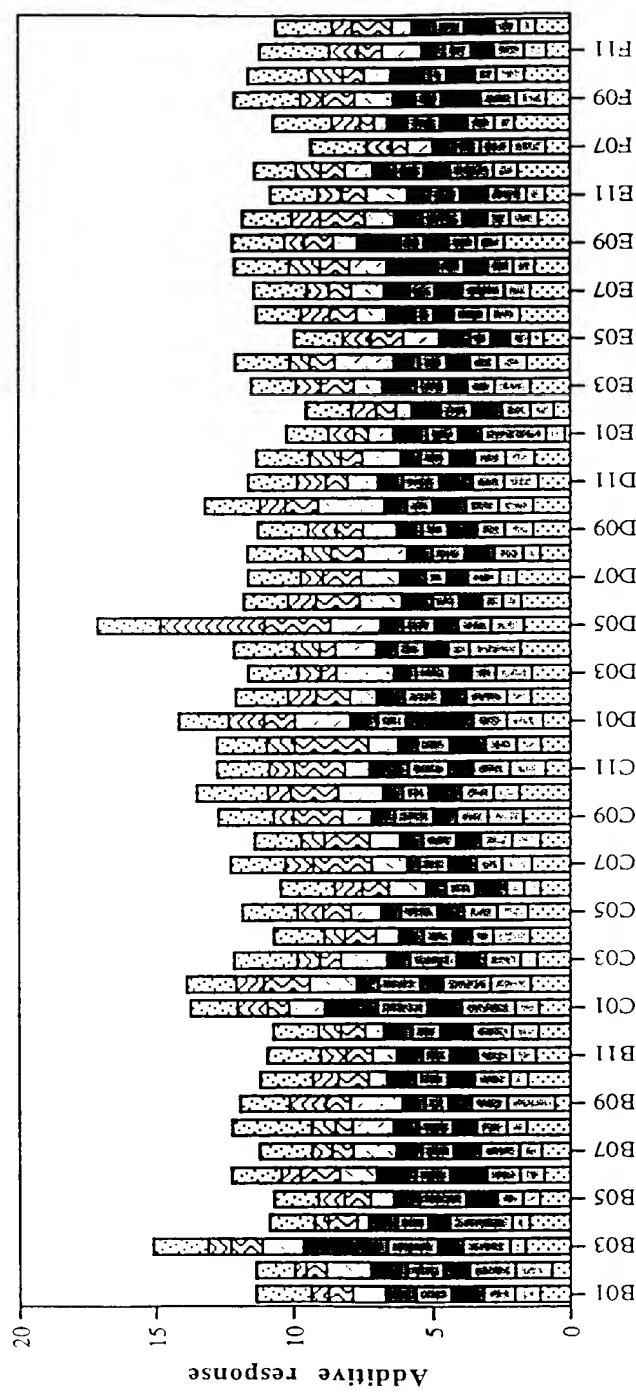


FIG. 5



1	A12	IKDFHVYFRESRDAG	49	E12	SATSRGVLVVAASGN
2	A11	LEQAVNSATSRGVLV	50	E11	SRGVLVVAASGNSGA
3	A10	AQSVPWGISRQAPA	51	E10	VLVVAASGNSGAGSI
4	A9	VPWGISRQAPAAHN	52	E9	VAASGNSGAGSISYP
5	A8	GISRVQAPAAHNRLG	53	E8	SGNSGAGSISYPARY
6	A7	RVQAPAAHNRLGTGS	54	E7	SGAGSISYPARYANA
7	A6	APAAHNRLGTGSGVK	55	E6	GSISYPARYANAMAV
8	A5	AHNRLGTGSGVKVAV	56	E5	SYPARYANAMAVGAT
9	A4	RGLTGSGVKVAVLDT	57	E4	ARYANAMAVGATDQN
10	A3	TGSGVKVAVLDTGIS	58	E3	ANAMAVGATDQNNNR
11	A2	GVKVAVLDTGISTHP	59	E2	MAVGATDQNNNRASF
12	A1	VAVLDTGISTHPDLN	60	E1	GATDQNNNRASFSQL
13	R12	LDTGISTHPDLNIRG	61	F12	DQNNNRASFSQLYQAG
14	B11	GISTHPDLNIRGGAS	62	F11	NNRASFSQLYQAGLDI
15	B10	THPDLNIRGGASFVP	63	F10	ASFSQYQAGLDIVAP
16	B9	DLNIRGGASFVPGEPE	64	F9	SQYQAGLDIVAPGVN
17	B8	IRGGASFVPGEPESTQ	65	F8	GAGLDIVAPGVNVQS
18	B7	GASFVPGEPESTQDGN	66	F7	LDIVAPGVNVQSTYP
19	B6	FVPGEPESTQDGNHG	67	F6	VAPGVNVQSTYPGST
20	B5	GEPSTQDGNHGHTHV	68	F5	GVNVQSTYPGSTYAS
21	B4	STQDGNHGHTHVAGT	69	F4	VQSTYPGSTYASLNG
22	B3	DGNHGHTHVAGTIAA	70	F3	TYPGSTYASLNGTSM
23	B2	GHGHTHVAGTIAALNN	71	F2	GSTYASLNGTSMATP
24	B1	THVAGTIAALNNSIG	72	F1	YASLNGTSMATPHVA
25	C12	AGTIAALNNSIGVLG	73	G12	LNGTSMATPHVAGAA
26	C11	IAALNNSIGVLGVP	74	G11	TSMATPHVAGAAALV
27	C10	LNNSIGVLGVAPSAE	75	G10	ATPHVAGAAALVKQK
28	C9	SIGVLGVAPSAELYA	76	G9	HVAGAAALVKQKNPS
29	C8	VLGVAPSAELYAVKV	77	G8	GAAALVKQKNPSWSN
30	C7	VAPSAELYAVKVLGA	78	G7	ALVKQKNPSWSNVQI
31	C6	SAELYAVKVLGASGS	79	G6	KQKNPSWSNVQIRNH
32	C5	LYAVKVLGASGGSV	80	G5	NPSWSNVQIRNHLKN
33	C4	VKVLGASGGSVSSI	81	G4	WSNVQIRNHLKNTAT
34	C3	LGASGGSVSSIAQG	82	G3	VQIRNHLKNTATSLG
35	C2	SGSGSVSSIAQGLEW	83	G2	RNHLKNTATSLGSTN
36	C1	GSVSSIAQGLEWAGN	84	G1	LKNTATSLGSTNLYG
37	D12	SSIAQGLEWAGNNGM	85	H12	TATSLGSTNLYGSGL
38	D11	AQGLEWAGNNGMHVA	86	H11	SLGSTNLYGSGLVNA
39	D10	LEWAGNNGMHVANLS	87	H10	STNLYGSGLVNAEAA
40	D9	AGNNGMHVANLSLGS	88	H9	NLYGSGLVNAEATR
41	D8	NGMHVANLSLGSPSP			
42	D7	HVANLSLGSPSPSAT			
43	D6	NLSLGSPSPSATLEQ			
44	D5	LGSPSPSATLEQAVN			
45	D4	PSPSATLEQAVNSAT			
46	D3	SATLEQAVNSATSRG			
47	D2	LEQAVNSATSRGVLV			
48	D1	AVNSATSRGVLVVA			

FIG. 6A

1	A12	IKDFHVYFRESRDAG	49	E12	KKIDVLNLSIGGPDF
2	A11	DAELHI FRVFTNNQV	50	E11	DVLNLSIGGPDFMDH
3	A10	PLRRASLSLGSGFWH	51	E10	NLSIGGPDFMDHPFV
4	A9	RASLSLGSGFWHATG	52	E9	IGGPDFMDHPFVDKV
5	A8	LSLGSGFWHATGRHS	53	E8	PDFMDHPFVDKVWEL
6	A7	GSGFWHATGRHSSRR	54	E7	MDHPFVDKVWELTAN
7	A6	FWHATGRHSSRRLLR	55	E6	PFVDKVWELTANNVI
8	A5	ATGRHSSRRLLRAIP	56	E5	DKVWELTANNVIMVS
9	A4	RHSSRRLLRAIPRQV	57	E4	WELTANNVIMVSAIG
10	A3	SRRLLRAIPRQVAQT	58	E3	TANNVIMVSAIGNDG
11	A2	LLRAIPRQVAQTLQQA	59	E2	NVIMVSAIGNDGPLY
12	A1	AIPRQVAQTLQADVL	60	E1	MVSAIGNDGPLYGTJ
13	B12	RQVAQTLQADVLWQM	61	F12	AIGNDGPLYGTLNNP
14	B11	AQTLQADVLWQMGYT	62	F11	NDGPLYGTLNNPADQ
15	B10	LQADVLWQMGYTGAN	63	F10	PLYGTLNNPADQMDV
16	B9	DVLWQMGYTGANVRV	64	F9	GTLNNPADQMDVIGV
17	B8	WQMGYTGANVRVAVF	65	F8	NNPADQMDVIGVGGI
18	B7	GYTGANVRVAVFDTG	66	F7	ADQMDVIGVGGIDFE
19	B6	GANVRVAVFDTGLSE	67	F6	MDVIGVGGIDFEDNI
20	B5	VRVAVFDTGLSEKHP	68	F5	IGVGGIDFEDNIARF
21	B4	AVFDTGLSEKPHFK	69	F4	GGIDFEDNIARFSSR
22	B3	DTGLSEKPHFKNVK	70	F3	DFEDNIARFSSRGMT
23	B2	LSEKPHFKNVKERT	71	F2	DNIARFSSRGMTTWE
24	B1	KPHFKNVKERTNWT	72	F1	ARFSSRGMTTWEPLG
25	C12	HFKNVKERTNWTNER	73	G12	SSRGMTTWEPLGGY
26	C11	NVKERTNWTNERLTD	74	G11	GMTTWEPLGGYGRMK
27	C10	ERTNWTNERLDDGL	75	G10	TWELPGGYGRMKPDI
28	C9	NWTNERLDDGLGHG	76	G9	LPGGYGRMKPDIVTY
29	C8	NERTLDDGLGHGT	77	G8	GYGRMKPDIVTYGAG
30	C7	TLDDGLGHGT	78	G7	RMKPDIVTYGAGVRG
31	C6	FVAGVIASMRE	79	G6	PDIVTYGAGVRGSGV
32	C5	GHGT	80	G5	VTYGAGVRGSGVKG
33	C4	FVAGVIASMRECQG	81	G4	GAGVRGSGVKGCR
34	C3	AGVIASMRECQGFAP	82	G3	VRGSGVKGCRALSG
35	C2	IASMRECQGFAPDAE	83	G2	SGVKGGCRALSGTSV
36	C1	MRECQGFAPDAELHI	84	G1	KGGCRALSGTSVASP
37	D12	CQGFAPDAELHI	85	H12	CRALSGTSVASPVVA
38	D11	FAPDAELHI	86	H11	LSGTSVASPVVAGAV
39	D10	FRVFTNNQVSYT	87	H10	TSVASPVVAGAVTLL
40	D9	DAELHI	88	H9	ASPVVAGAVTLLVST
41	D8	FRVFTNNQVSYT	89	H8	VVAGAVTLLVSTVQK
42	D7	FTNNQVSYT	90	H7	GAVTLLVSTVQKREL
43	D6	SWFLDAFN	91	H6	TLLVSTVQKRELVNP
44	D5	SYT	92	H5	VSTVQKRELVNPASM
45	D4	SWFLDAFN	93	H4	VQKRELVNPASMQQA
46	D3	LDAFN	94	H3	RELVNPASMQALIA
47	D2	FNYAILKKIDVL	95	H2	VNPASMQALIASAR
48	D1	AILKKIDVLNLSIGG	96	H1	ASMKQALIASARRLP

FIG. 6B

97	I12	IKDFHVYFRESRDAG
98	I11	DAELHI FRVFTNNQV
99	I10	KQALIASARRLPGVN
100	I9	LIASARRLPGVNMFE
101	I8	SARRLPGVNMFEQGH
102	I7	RLPGVNMFEQGHGKL
103	I6	GVNMFEQGHGKLDLL
104	I5	MFEQGHGKLDLLRAY
105	I4	QGHGKLDLLRAYQIL
106	I3	GKLDLLRAYQILNSY
107	I2	DLLRAYQILNSYKPQ
108	I1	RAYQILNSYKPQASL
109	J12	QILNSYKPQASLSPS
110	J11	NSYKPQASLSPSYID
111	J10	KPQASLSPSYIDLTE
112	J9	ASLSPSYIDLTECPY
113	J8	SPSYIDLTECPYMWP
114	J7	YIDLTECPYMWPYCS
115	J6	LTECPYMWPYCSQPI
116	J5	CPYMWPYCSQPIYYG

FIG. 6C

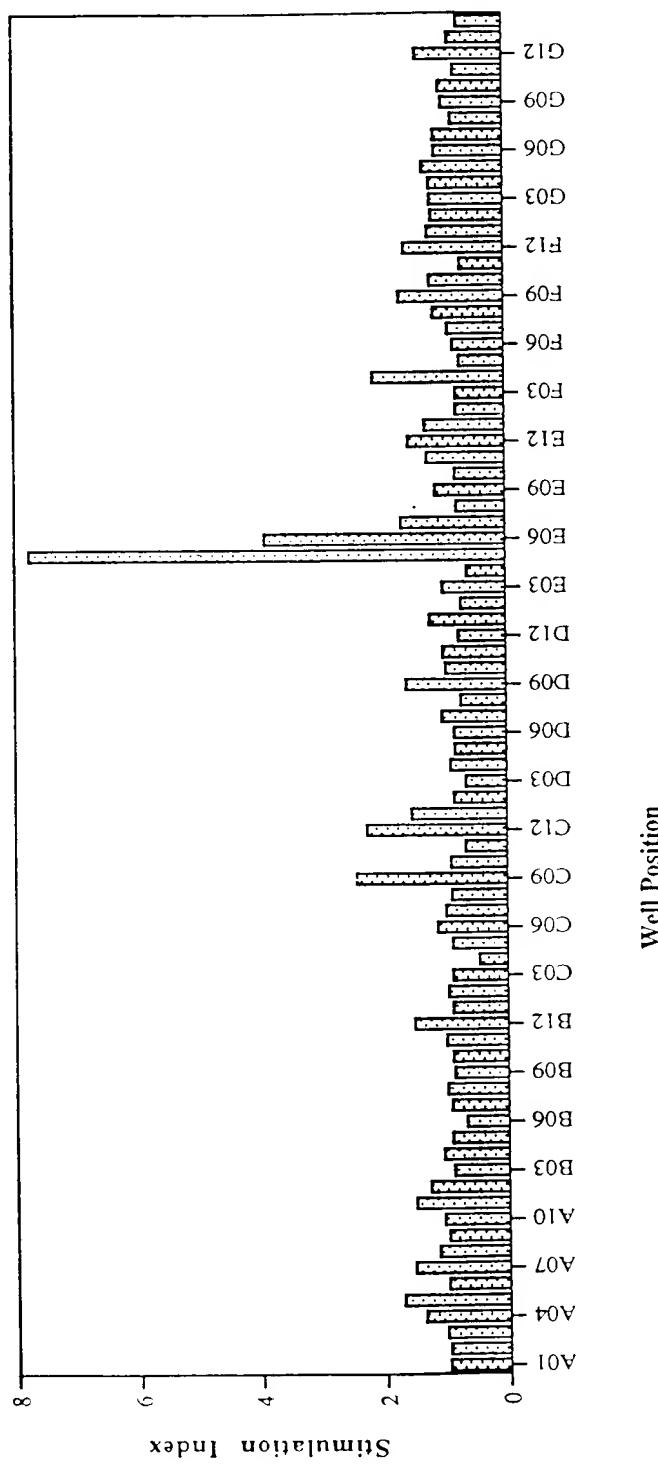
MKLVNIWLLLLVVLLCGKKHLGDRLEKKSFEKAPCPGCSHLTLKVEFSSTVVEYEYIVAFNGYFT
AKARNSFISSALKSSEVDNWRIIPRNNPSSDYP PSDFEVIQIKEQKAGLLTLEDHPNIKRVTPQR
KVFRLKYAESDPTVPCNETRWSQWQSSRPLRRASLSLGSGFWHATGRHSSRLLRAIPRQVAQ
TLQADVLWQMGYTGANVRVAVFDTGLSEKPHFKNVKERTNWTNERTLDDGLGHGTFVAGVIASM
RECQGFAPDAELHIFRVFTNNQSYTWSFLDAFNYAILKKIDVLNLSIGGPDFMDHPFVDKVWEL
TANNVIMVSAIGNDGPLYGTLNTPADQMDVIGVGGIDFEDNIARFSSRGMTTWELPGGYGRMKPD
IVTYGAGVRGSGVKGGCRALSGTSVASPVVAGAVTLLVSTVQKRELVNPASMKQALIASARRLPG
VNMFEQGHGKLDLLRAYQILNSYKPQASLSPSYIDLTECPYMWPYCSQPIYYGGMPTVVNVTILN
GMGVGTRIVDKPDWQPYLPQNGDNIEVAFSYSSVLWPWSGYLAISISVTKKAASWEGLAQGHVMI
TVASPAETESKNGAEQTSTVKLPIVKIIIPTPPRSKRVLWDQYHNLRYPPGYFPRDNLRMKNDPL
DWNGDHIHTNFRDMDYQHLRSMGYFVEVLGAPFTCFDASQYGTLLMDSEEEYFPEEIAKLRRDVD
NGLSLVIFSDWYNTSVMRKVKFYDENTRQWWMPDTGGANIPALNELLSVWNMGFS DGLYEGEFTL
ANHDMDYYASGCSIAKFPEDGVVITQTFKDQGLEVLKQETAVVENVPILGLYQIPAEGGGRIVLYG
DSNCLDDSHRQKDCFWLLDALLQYTSYGVTPPSLSHSGNRQRRPSGAGSVTPERMEGNHLHRYSK
VLEAHLGDPKPRPLPACPRLSWAKPQPLNETAPSNLWKHQKLLSIDLDKVLPNFRSNRPQVRPL
SPGESGAWDI PGGIMPGRYNQEVGQTIPVFAFLGAMVVLAFFVVQINKAKSRPKRRKPRVKRQPL
MQQVHPPKTPSV

FIG. 7

	10	20	30	40	50	
BPN'	A Q S V P Y G V S Q - I K A P A L H S Q G Y T G S N V K V A V I D S G I D S S H P D L K - V A G G A					48
SAVINASE	A Q S V P W G I S R - V Q A P A A H N R G L T G S G V K V A V L D T G I - S T H P D L N - I R G G A					47
S2HSBT	- R A I P R Q V A Q T L Q A D V L W Q M G Y T G A N V R V A V F D T G L S E K H P H F K N V K E R T					49
	60	70	80	90	100	
BPN'	S M V P S E T N P F Q D N N S H G T H V A G T V A A L N N S I G V L G V A P S A S L Y A V K V L G A					98
SAVINASE	S F V P G E P S T - Q D G N G H G T H V A G T I A A L N N S I G V L G V A P S A E L Y A V K V L G A					96
S2HSBT	N W - - T N E R T L D D G L G H G T F V A G V I A S M R E C Q G F - - - A P D A E L H I F R V F T N					94
	110	120	130	140	150	
BPN'	D G S G Q Y S W I I N G I E W A I A N N M D V I N M S L G G P S - G S A A L K A A V D K A V A S G V					147
SAVINASE	S G S G S V S S I A Q G L E W A G N N G M H V A N L S L G S P S - P S A T L E Q A V N S A T S R G V					145
S2HSBT	N Q V S Y T S W F L D A F N Y A I L K K I D V L N L S I G G P D F M D H P F V D K V W E L T A N V					144
	160	170	180	190	200	
BPN'	V V V A A A G N E G T S G S S S T V G Y P G K Y P S V I A V G A V D S S N Q R A S F S S V G P E L -					197
SAVINASE	L V V A A S G N S G A - - - G S I S Y P A R Y A N A M A V G A T D Q N N N R A S F S Q Y G A G L -					191
S2HSBT	I M V S A I G N D G P - - L Y G T L N N P A D Q M D V I G V G G I D F E D N I A R F S S R G M T T W					192
	210	220	230	240	250	
BPN'	----- D V M A P G V S I Q S T L P G N K Y G A Y N G T S M A S P H V A G A A L I L					235
SAVINASE	----- D I V A P G V N V Q S T Y P G S T Y A S L N G T S M A T P H V A G A A A L V K					229
S2HSBT	E L P G G Y G R M K P D I V T Y G A G V R G S G V K G G C R A L S G T S V A S P V V A G A V T L L V					242
	260	270	280	290		
BPN'	S K H P N W T N T Q - - - V R S S L E N T T T K L G D S F Y Y G K G L I N V Q A A A Q					275
SAVINASE	Q K N P S W S N V Q - - - I R N H L K N T A T S L G S T N L Y G S G L V N A E A A T R					269
S2HSBT	S T V Q K R E L V N P A S M K Q A L I A S A R R L P G V N M F E Q G - - - H G K L					280

FIG. 8

FIG. 9



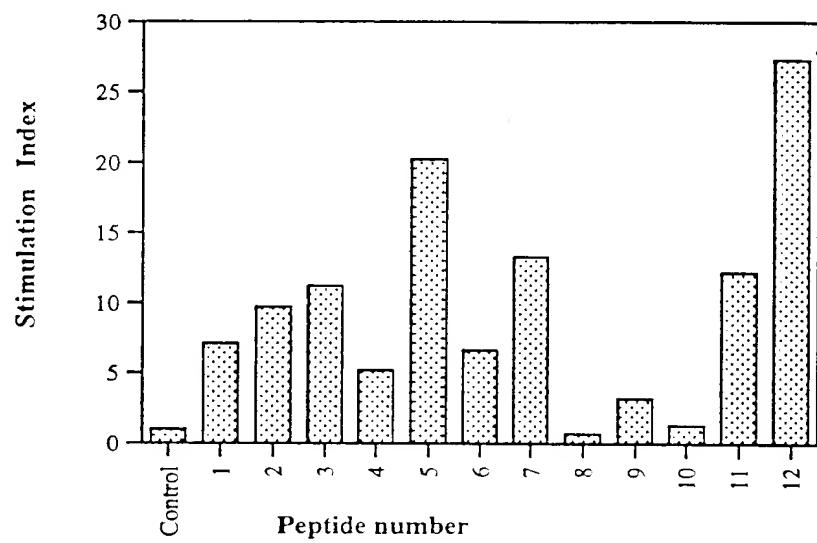
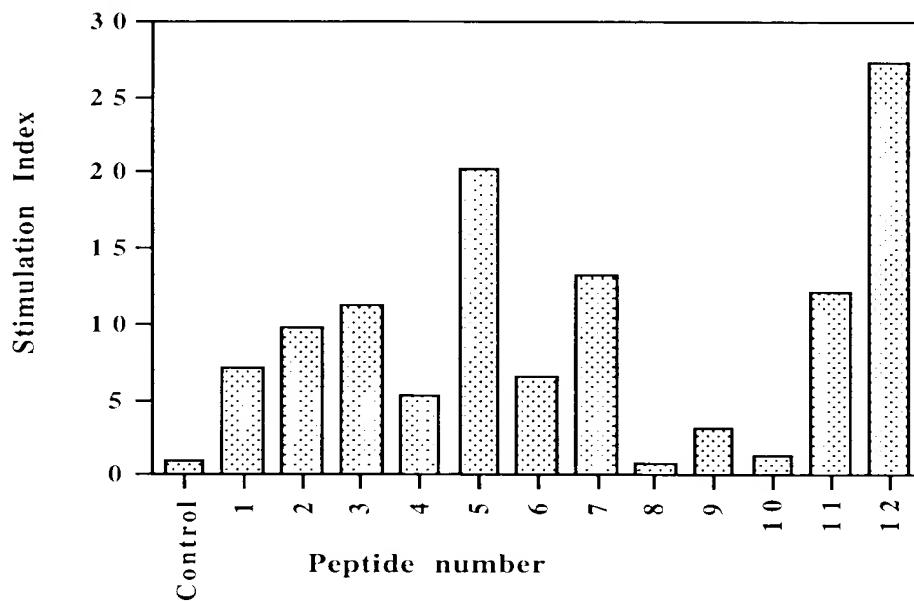


FIG. 10



Peptide number	Sequence
1 (unmodified sequence)	GSISYPARYANAMAV
2	ASISYPARYANAMAV
3	GAISYPARYANAMAV
4	GSASYPARYANAMAV
5	GSIAYPARYANAMAV
6	GSISAPARYANAMAV
7	GSISYAARYANAMAV
8	GSISYPAAYANAMAV
9	GSISYPARAANAMAV
10	GSISYPARYAAAMAV
11	GSISYPARYANAAAV
12	GSISYPARYANAMAA

FIG. 11

Human subtilisin percent responders

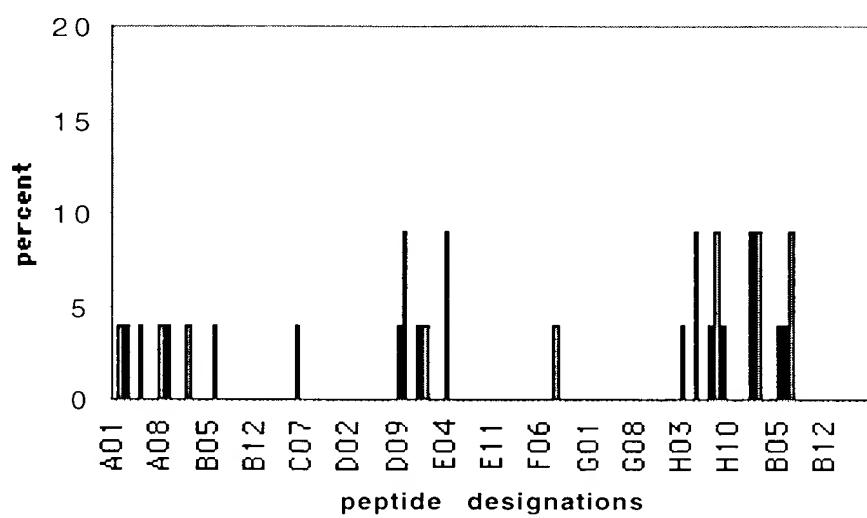


FIG. 12

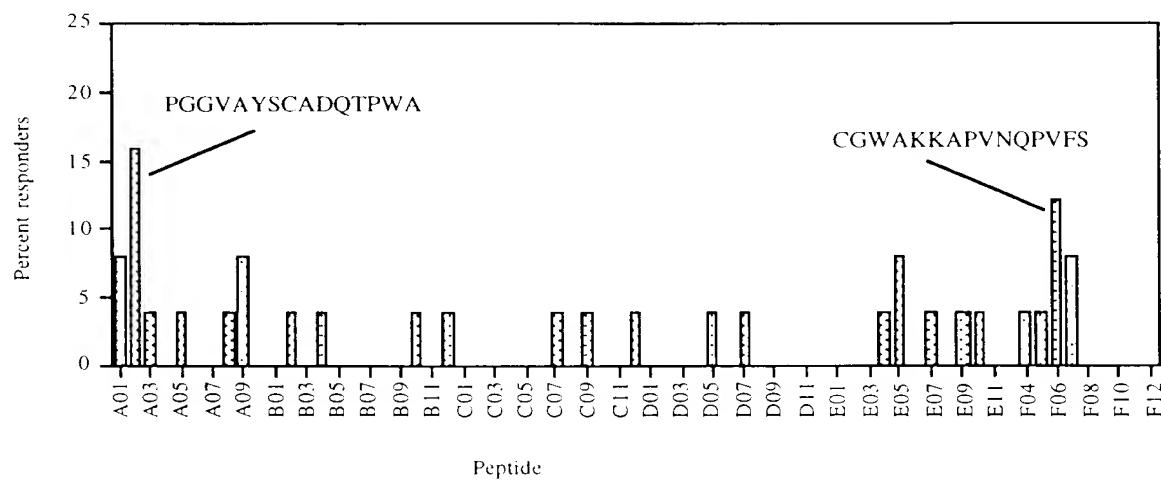


FIG. 13A

1	2	3	4	5
1234567890	1234567890	1234567890	1234567890	1234567890
MRSSPLLPSA	VVAALPVIAL	AADGRSTRYW	DCCKPSCGWA	KKAPVNQPVF
<u>SCNANFQRIT</u>	DFDAKSGCEP	<u>GGVAYSCADQ</u>	<u>TPWAVNDDFA</u>	LGFAATSIA
SNEAGWCCAC	YELTFTSGPV	AGKKMVVQST	STGGDLGSNH	FDLNI PGGGV
GIFDGCTPQF	GGLPGQRYGG	ISSRNECDRF	PDALKPGCYW	RFDWFKNADN
PSFSFRQVQC	PAELVARTGC	RRNDDGNFPA	VQIPSSSTSS	PVNQPTSTST
TSTSTTSSPP	VQPTTPSGCT	AERWAQ		

FIG. 13B

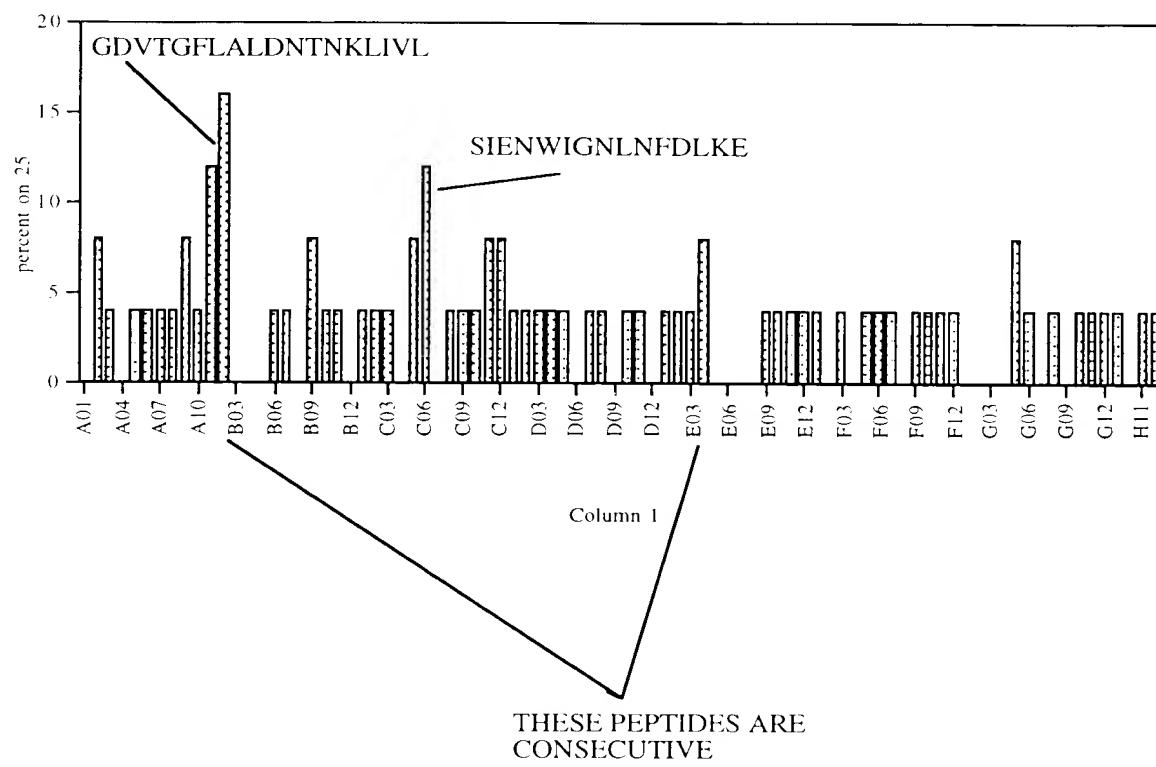


FIG. 14A

1 mrsslvlfv sawtalaspi rrevsqdlfn qfnlfaqysa aaycgknnda
51 pagtnitctg nacpevekad atflysfeds **gvqdvtqfla ldntnklivl**
101 sfrgsrsien **wignlnfdlk eindicsgcr** ghdgftsswr svadtlrqkv
151 edavrehpdy rvvftghs1g galatvagad lrgngydidv fsygaprvgn
201 rafaefltvq tgglyrith tndivprlpp refgyshssp eywiksgtlv
251 pptrndivki egidatggnn qpnipdipah lwyfgligtc 1

FIG. 14B

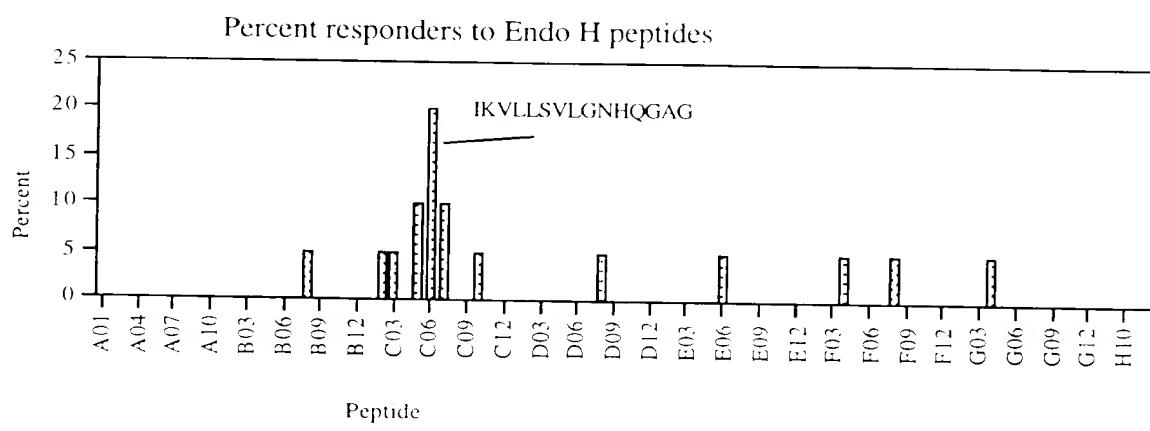


FIG. 15A

1 mftpvrrrvr taalalsaaa alvlgstaas gasatpspap apapapvkqg
51 ptsvayvevn nnsmlnvgky tladgggnaf dvavifaani nydtgtktay
101 lhfnenvqrv ldnavtqirp lqqqg*ikvll* svlqnhqqag fanfpsqqaa
151 safakqlsda vakygldgvd fddeyaeygn ngtaqpndss fvhltalra
201 nmpdkiisly nigpaasrls yggvdvsdkf dyawnpyygt wqvgialpk
251 aqlspaavei grtsrstvad larrtvdegy gvyltynldg gdrtadvsaf
301 trelygseav rtp

FIG. 15B

BPN compiled for 22 individuals.

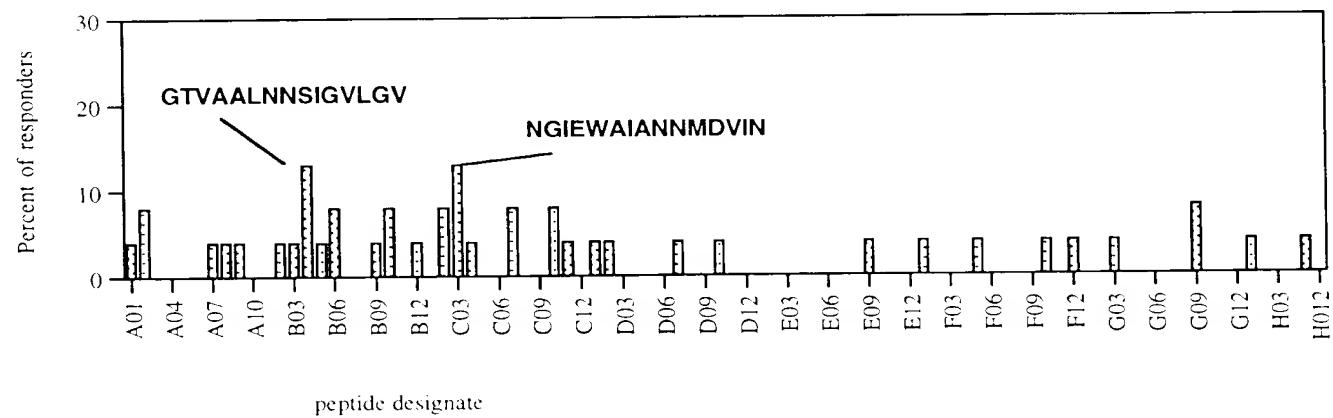


FIG. 16

GG36 percent responders

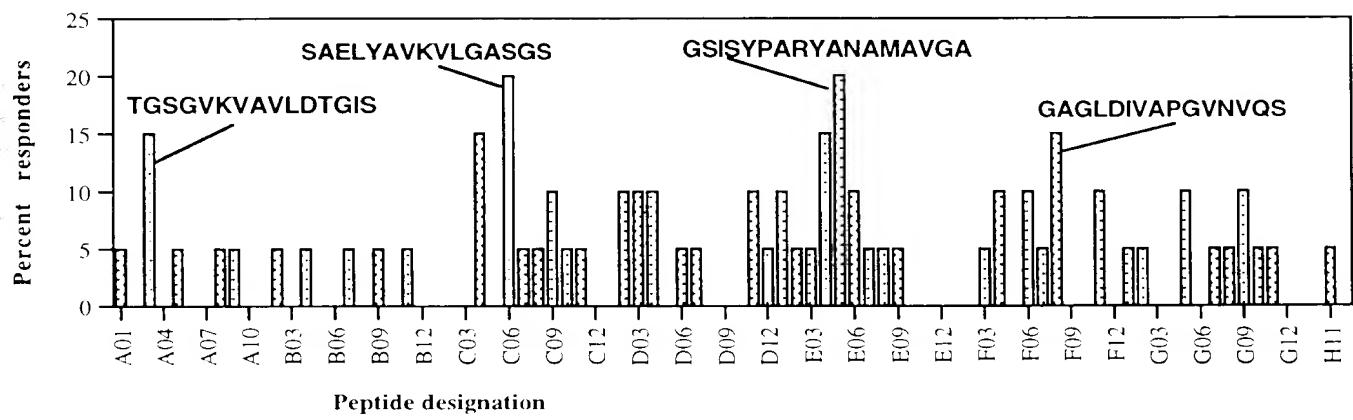


FIG. 17

Hybrid enzyme sequence (GG36-BPN)

GG36

AQSVPWGISRQAPAAHNRLTGSGVKVAVLDTGISTHPDLNIRGGASFVPGEPTQDGNGH

BPN

GTHVAGTIAALNNSIGVLGVAPS AELYAVKVLGASGSGSVSSIAQGLEWAGNNGMHVINMSLGGS

△

GSAALKAAVDKAVASGVVVVAAAGNEG TGS SSVGYPGK YPSVIAVGAVDSSNQRASFSSVGP

ELDVMAPGVSIQSTLPGNKYGAYNGTSMASPHVAGAAALILSKHPNWTNTQVRSSLENTTKLGD

SFYY GKGLINVQAAAQ

FIG. 18